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Amendments to the claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

1. (currently amended) A method of detecting whether a subject is either predisposed to or afflicted with a pulmonary disease hypertension which comprises (1) obtaining a suitable sample from the subject; and (2) detecting in the sample a bone morphogenetic protein receptor-II mutation which is not present in a suitable sample of wildtype bone morphogenetic protein receptor-II,

wherein the presence of a mutation indicates that the subject is predisposed to or afflicted with the pulmonary disease hypertension.

- 2. (currently amended) The method of claim 1, wherein the suitable sample is a comprises nucleic acid sample, and the mutation is detected in a nucleic acid molecule encoding bone morphogenetic protein receptor-II.
- 3. (currently amended) The method of claim 1, wherein the suitable sample is one which comprises a bone morphogenetic protein receptor-II polypeptide, and the mutation is detected in the bone morphogenetic protein receptor-II polypeptide.

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- 4. (currently amended) The method of claim 1, wherein the pulmonary disease hypertension is Primary Pulmonary Hypertension.
- 5. (original) The method of claim 4, wherein the Primary Pulmonary Hypertension is Familial Primary Pulmonary Hypertension.
- 6. (previously canceled)
- 7. (canceled)
- 8. (canceled)
- 9. (previously canceled)
- 10. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a deletion of a nucleotide segment guanosine-guanosine-guanosine-guanosine-adenosine located at positions 1099-1103 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 11. (original) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at a glutamic acid

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residue located at position 368 in the wildtype polypeptide, which wildtype polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2.

- 12. (currently amended) The method of claim 2, wherein the mutated nucleic acid <u>molecule</u> comprises a deletion of a thymidine residue located at position 2579 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in Seq SEQ ID NO:1.
- 13. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at an asparagine residue located at position 861 in the wildtype polypeptide, which wildtype polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2.
- 14. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a replacement of a nucleotide segment cytosine-thymidine-thymidine-thymidine thymidine located at positions 507-510 in a wildtype nucleic acid with a nucleotide segment adenosine-adenosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 15. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a mutation of a cysteine located at position 169 in a

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wildtype polypeptide to a termination codon, which wildtype polypeptide comprises the sequence set forth in SEO ID NO:2.

- 16. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a cytosine located at position number 2617 in a wildtype nucleic acid to a thymidine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 17. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a mutation of an arginine located at position 873 in a wiltype polypeptide to a termination codon, which wildtype polypeptide comprises the sequence set forth in SEQ ID NO:2.
- 18. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a replacement of a nucleotide segment adenosine-guanosine present at positions 690-691 in a wildtype nucleic acid with a thymidine residue, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 19. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at a lysine residue located at position 230 in a wildtype polypeptide, which wildtype

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polypeptide comprises the sequence set forth in SEQ ID NO:2.

- 20. (previously canceled)
- 21. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a cytosine located at position number 1471 in a wildtype nucleic acid to a thymidine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 22. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a mutation of an arginine located at position 491 in a wildtype polypeptide to a tryptophan, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 23. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a guanosine located at position number 1472 in a wildtype nucleic acid to an adenosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 24. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide polypeptide comprises a mutation of an arginine located at position number 491 in a wildtype

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polypeptide to a glutamine, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.

- 25. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a deletion of a nucleotide segment adenosine-thymidine-thymidine-thymidine located at positions 1248-1251 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 26. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of an phenylalanine located at position number 417 in a wildtype polypeptide to a stop codon, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 27. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a cytosine located at position number 994 in a wildtype nucleic acid to a thymidine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 28. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of an arginine located at position number 332 in a wildtype polypeptide to a

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stop codon, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.

- 29. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a thymidine located at position number 295 in a wildtype nucleic acid to a cytosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 30. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of a cysteine located at position number 99 in a wildtype polypeptide to an arginine, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 31. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a deletion of a guanosine residue located at position 1097 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in Seq SEQ ID NO:1.
- 32. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at a proline residue located at position 366 in the wildtype polypeptide, which wildtype polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2.

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- 33. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a guanosine located at position number 727 in a wildtype nucleic acid to a thymidine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 34. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of a glutamic acid located at position number 243 in a wildtype polypeptide to a stop codon, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 35. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a deletion of an adenosine residue located at position 1214 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in Seq SEQ ID NO:1.
- 36. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at an aspartic acid residue located at position 405 in the wildtype polypeptide, which wildtype polypeptide comprises the amino acid sequence set forth in SEO ID NO:2.
- 37. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a deletion of a

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nucleotide segment adenosine-cytosine located at positions 2441-2442 in a wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.

- 38. The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypeptide comprises a frameshift mutation at a histidine residue located at position 814 in the wildtype polypeptide, which wildtype polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2.
- 39. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a cytosine located at position number 2695 in a wildtype nucleic acid to a thymidine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 40. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of an arginine located at position number 899 in a wildtype polypeptide to a stop codon, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 41. (currently amended) The method of claim 2, wherein the mutated nucleic acid <u>molecule</u> comprises a deletion of a nucleotide segment present at positions 189-209 in a

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wildtype nucleic acid, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.

- 42. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a deletion of an amino acid segment serine-threonine-cysteine-tyrosine-glycine-leucine-tryptophan located at position numbers 64-70 in a wildtype polypeptide, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 43. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a guanosine located at position number 296 in a wildtype nucleic acid to a adenosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 44. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of a cysteine located at position number 99 in a wildtype polypeptide to a tyrosine, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 45. (currently amended) The method of claim 2, wherein the mutated nucleic acid <u>molecule</u> comprises a mutation of a thymidine located at position number 250 in a wildtype

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nucleic acid to a cytosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.

- 46. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of a cysteine located at position number 84 in a wildtype polypeptide to an arginine, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 47. (currently amended) The method of claim 2, wherein the mutated nucleic acid molecule comprises a mutation of a guanosine located at position number 1040 in a wildtype nucleic acid to a adenosine, which wildtype nucleic acid comprises the sequence set forth in SEQ ID NO:1.
- 48. (currently amended) The method of claim 3, wherein the mutated bone morphogenetic protein receptor-II polypepetide polypeptide comprises a mutation of a cysteine located at position number 347 in a wildtype polypeptide to a tyrosine, which wildtype polypeptide has the sequence set forth in SEQ ID NO:2.
- 49. The method of claim 5, wherein the subject is suffering from an asthmatic symptom, so as to thereby prevent a subject afflicted with Familial Primary Pulmonary Hypertension from being misdiagnosed as asthmatic.

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50. (previously canceled)

- 51. (currently amended) A method of predicting an increased likelihood of a subject giving birth to twins or triplets which comprises:
 - a) obtaining a suitable nucleic acid sample from the subject;
 - b) detecting the presence of one copy of a mutant nucleic acid <u>molecule</u> which encodes a bone morphogenetic protein receptor-II polypeptide, thereby indicating that the subject is heterozygous for the mutation,

wherein heterozygosity predicts an increased likelihood of the subject giving birth to twins or triplets.

- 52. (currently amended) A method of predicting an increased likelihood of a subject having a miscarriage prior to giving birth to a child which comprises:
 - a) obtaining a suitable nucleic acid sample from the subject;
 - b) detecting the presence of two copies of a mutant nucleic acid <u>molecule</u> which encodes a bone morphogenetic protein receptor-II polypeptide, thereby indicating that the subject is homozygous for the mutation,

wherein homozygosity predicts an increased likelihood of the subject having a miscarriage prior to giving birth to a child.

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- 53. (withdrawn)
- 54. (previously canceled)
- 55. (withdrawn)
- 56. (allowed) A method of detecting whether a subject is either predisposed to or afflicted with Familial Primary Pulmonary Hypertension which comprises:
 - a) obtaining a suitable nucleic acid sample from the subject; and
 - b) detecting the presence of a $(GGC)_{12}$ trinucleotide repeat at positions -928 to -963 in the 5' end of the bone morphogenetic protein receptor-II gene,

wherein the presence of the trinucleotide repeat indicates that the subject is either predisposed to or afflicted with Familial Primary Pulmonary Hypertension.

- 57. (withdrawn)
- 58. (previously canceled)
- 59-60. (withdrawn)
- 61-63. (previously canceled)